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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,744	01/30/2004	Anna Helgadottir	30847/2051-004	6429

4743 7590 12/19/2008

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	**PAPER NUMBER**
1618	
MAIL DATE	**DELIVERY MODE**
12/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/769,744	HELGADOTTIR ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *206-228* is/are pending in the application.

4a) Of the above claim(s) *210,215 and 218-224* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *206-209,211-214,216,217 and 225-228* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/03/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on **9/15/08** has been entered.

2. Applicant's argument filed 9/15/08 has been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 206-228 are pending, claims 206-209, 211-214, 216-217 and 225-228 are rejected in this office action. Claims 210, 215, 218-224 are withdrawn.

5. The rejection of claims 212 and 213 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn due to the amendment of the claims.

6. The information disclosure statement (IDS) submitted on 12/03/08 have been received and acknowledged.

7. Claims 206-209, 211-214, 216-217 & 226 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hatzelmann et al. (1994) and Mazzone et al. (2001) and Pietila (1996) in view of Rossoni et al. (1996) and Muller-Peddinghaus et al. and

Gompertz et al. (2002) and Cunningham et al. (1997) for the reasons made of record in Paper No. 20080313 and as follows.

Applicant argues specific steps are required such as selecting a human subject at risk of MI. Applicant also argues that the rejection is based on seven references". Applicant also argues that "Hatzelmann does not teach or describe studies with patients or treatment regimen" and does not teach or describe oral administration. Applicant then argues that Pietila et al. "only concluded that CRP levels may play a role in selecting MI patients for therapies" and "that thrombolytic drugs are administered to dissolve blood clots." Applicant further argues that the "combination of Hatzelmann, Mazzone and Pietila is not obvious" and specifically that "Mazzone makes clear that silent versus symptomatic ischemia have different cytokine profiles and neither population is equivalent to post infarction population studies by Pietila". Applicant finally requests that the "Examiner should explain why the above three documents would have been chosen and combined by one of ordinary skill in the art".

In response, with regards to selecting the patient population at risk of having a heart attack, everyone is at risk of having a MI; there is no human that is not at risk of having a heart attack. In addition, claims 207, 214, 216-217 and 225-228 needed to be better explained and therefore additional references were employed to make this obvious and clear. It is noted that reliance on a large number of references in a rejection does not negate an obviousness rejection. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). Applicant should note that a document "as evidence

by" is merely used to support Examiners view point. Therefore, in fact, only 4 references were actually part of the rejection.

Contrary to Applicant's assertion that Hatzelmann fails to teach studies with patients or a treatment regimen, or that the drug BAY-X-1005 is not administered orally by Hatzelmann, Hatzelmann teaches oral administration of BAY-X-1005 to patients suffering from inflammatory disease. See page 64, conclusion, lines 1-5, 10-15 from the bottom, also see page 65, left col. last 4 lines bridging right col. line 1 (i.e., inclusive of a population at risk of MI, because everyone is at risk of having a heart attack), wherein it is further disclosed that the binding site and inhibition of leukotriene synthesis in humans and rats PMNL are of high affinity. Applicant should also note that Hatzelmann is not a review article as indicated on page 12 of the remarks.

In summary, Hatzelmann et al. teach oral administration of BAY-X-1005, the claimed compound, for the inhibition of inflammatory disease. Hatzelmann teaches that BAY-X-1005 is a binding leukotriene synthase inhibitor, and thus inhibits leukotriene synthesis and will intrinsically reduce serum CRP protein when administered because "products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Further, as correctly stated by Applicant, Hatzelmann teaches an investigation of the biochemical/pathway role of FLAP. Therefore one of ordinary

skill in the art would have been motivated to further investigate the inhibition of FLAP with the claimed compound (i.e. as it relates to claim 206).

However, Hatzelmann is silent regarding a population "at risk for MI". For that reason, Mazzone and Pietila were introduced to show that inflammation is myocardial ischemic correlates to inflammation, and that C-reactive protein (CRP) is one of the acute phase proteins that increase during systemic inflammation.

Pietila was used as an evidence to show that in MI, CRP levels may play a role in patient's selection MI therapies as required by instant claim 206. Arguments that Pietila focuses on thrombolytic treatment is found not persuasive, because a cardiologist knows that thrombolysis occurs in MI, and because Pietila specifically teach that MI is a cause of high CRP. Thus a drug that will inhibit leukotriene synthesis will intrinsically reduce the CRP level in a MI patient. Pietila et al. finally teach that C-reactive protein is evidence of acute myocardial infarction. Thus, the teachings of Hatzelmann become clearer when considered with the teachings of Mazzone and Pietila to treat patients at risk of MI by administering the compound of Hatzelmann.

As also evidence by Ridker et al. (Circulation (1998) 98:839-844), Ridkar teaches that recent prospective data demonstrates that low-grade inflammation, as assessed by C-reactive protein (CRP), predicts risk of first myocardial infarction and other atherosclerotic events among apparently healthy middle-aged men. In addition, CRP appears to predict risks of infarction and coronary death among high-risk patients as well as ischemic complications among those with stable and unstable angina.

Applicant should note that the only limitation that is silent in Hatzelmann is the population at risk for MI. All other limitations such as reducing CRP, inhibiting FLAP are met intrinsically because as stated above the property of the compound will remain the same. Therefore Examiner has shown the relationship between MI and CRP via Mazzone and Pietila. Applicant's assertion that neither Pietila or Mazzone or Hatzelmann draw a connection between leukotriene and CRP or even suggest using a leukotriene inhibitor to reduce CRP is not given a weight because the only requirement recited in the claims is for the compound to be administered to patients "at risk of MI" (see page 15 para. 2). As stated above, once the compound is administered to patients with inflammatory disease, wherein inflammatory disease is related to MI via CRP, inhibiting leukotriene and reducing serum CRP would be part of the property function of the compound.

Rossoni is directed to treating a mammal at "risk of MI' in an animal model; thereby further suggesting and expanding the teachings of Hatzelmann. As it is well established in the scientific arena, preclinicals are done through animal model mimicking humans.

Lastly, there is no need to reiterate that BAY-X-1005 is an inhibitor because the property of a compound cannot be stripped off from a compound's structure. Note the Examiner incorporated Gompertz and Cunningham to show the nexus between BAY-X-1005 and reducing leukotrienes.

8. Claims 225, 227-228 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hatzelmann et al. (1994) and Mazzone et al. (2001) and Pietila (1996) in view of Rossoni et al. (1996) and Muller-Peddinghaus et al. and Gompertz et al. (2002) and Cunningham et al. (1997) as applied to claims **206-209, 211-213, 216-217 and 226** above further in view of Byrum et al. (1997).

Hatzelmann et al., Mazzone et al., Pietila et al., Rossoni et al. Muller-Peddinghaus et al., Gompertz et al. are applied as above.

Applicant argues that the claims are directed to determining the FLAP genotype or haplotype of a human subject and selecting for treatment of a human subject with a FLAP gene.

In response, only claim 225 recites any recitation related to determining a FLAP genotype or haplotype. Note also that Byrum had used animal models to show a relationship of FLAP genotype to inflammation. Byrum et al. was introduced to show that when a FLAP genotype is missing, a reduced inflammatory response is seen, as discussed in the last office action. Although Byrum et al. did not teach explicitly the determination of Flap genotype in humans, Byrum teaches identification of the FLAP genes in animals (mice) and showed that when the genotype is missing, reduced inflammatory response is seen (see page 1073).

9. Applicants' request that the **Double Patenting** rejection be held in abeyance until it is made permanent is noted, but will be maintained in this Office Action and future Office Actions until withdrawn. Applicants have not presented a terminal disclaimer and

the claims of the above co-pending rejection remain pending, since this is not the only or sole rejection remaining the rejection is properly maintained.

Claims 206-209, 211-214, 216-217 and 225-228 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1-7, 25-31 and 32-41** of U.S. Patent Application No. **11270804**. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons made of record in Paper no. 20080313.

10. Claims 206-209, 211-214, 216-217 and 225-228 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1, 4-5, 7-9, 11-12, 23-25, 37, 40 and 43-45** of U.S. Patent Application No. **10587412**. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons made of record in Paper no. 20080313.

11. Claims 206-209, 211-214, 216-217 and 225-228 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 206-210, 212-222, and 245-246 of Patent Application No. 10830477. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons made of record in Paper no. 20080313.

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1618
12/11/08

/Robert C. Hayes/
Primary Examiner, Art Unit 1649